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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,064	04/21/2004	Andreas Weichert	DEAV2003/0029 US NP	6253

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/829,064	WEICHERT ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) 1-7 is/are allowed.

6)☒ Claim(s) 8 and 9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4-21-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-9 are pending.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Scope of Enablement: Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being **enabling** for a method of treating the following diseases:

cardiovascular diseases, stable or unstable angina pectoris, coronary heart disease, Prinzmetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, endothelial dysfunction, atherosclerosis, endothel damage after PTCA, hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension,

does **not** reasonably provide **enable**ment for a method of treating the following disease:

thrombosis, peripheral artery occlusive disease, restenosis, chronic glomerulonephritis, erectile dysfunction, ventricular arrhythmia, diabetes, diabetes complications, nephropathy, retinopathy, angiogenesis, asthma bronchiale, chronic renal failure, cirrhosis of liver, osteoporosis, restricted memory performance or a restricted ability to learn.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 8 recites: "*A method for the stimulation of the expression of endothelial NO synthase...comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1.*" Said method includes the treatment of many known diseases as well as those that are yet to be discovered. Therefore, the scope of claim 8 is unduly broad.

Claim 9 recites: "*A method for the treatment of cardiovascular diseases, stable or unstable angina pectoris, coronary heart disease, Prinzmetal angina, acute coronary syndrome, heart failure, myocardial infarction, stroke, thrombosis, peripheral artery occlusive disease, endothelial dysfunction, atherosclerosis, restenosis, endothel damage after PTCA, hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, renovascular hypertension, chronic glomerulonephritis, erectile dysfunction, ventricular arrhythmia, diabetes, diabetes complications, nephropathy, retinopathy, angiogenesis, asthma bronchiale, chronic renal failure, cirrhosis of liver, osteoporosis, restricted memory performance or a restricted*

ability to learn, or for lowering of cardiovascular risk of postmenopausal women or after intake of contraceptives, in a patient in need thereof, comprising administering to the patient a pharmaceutically effective amount of a compound according to claim 1." As evident by a large number of unrelated diseases, the scope of claim 9 is also unduly broad.

The amount of direction or guidance presented:

In the specification, the *in-vitro* and *in-vivo* assays only provide evidence for the treatment of atherosclerosis and cardiovascular diseases or related disorders (e.g., various forms of hypertension or angina), and coronary disease only. The specification does not provide the following:

- Blood glucose reduction for the treatment of diabetes;
- Bone density for the treatment of osteoarthritis;
- Inhibition of abnormal cellular proliferation for the treatment of angiogenesis;
- Renal function for the treatment of chronic glomerulonephritis or chronic renal failure;
- Liver function for the treatment of cirrhosis; etc.

Thus, the specification does not provide sufficient enablement to guide one skilled in the art to use the claimed compounds in the treatment of various diseases claimed herein.

The state of the prior art:

As evident by the teaching of **Martin-Santamaria et. al.** (cited on IDS), the claimed tricyclic core possesses potent antitumor activity, and nothing else. Thus, the state of the art does not support the various treatments recited in the instant claims 8 and 9.

The relative skill of those in the art:

Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the use of the claimed compounds in the treatment of various unrelated diseases such as: cardiovascular diseases, diabetes, cirrhosis, asthma, angiogenesis, renal failure, etc. Such a task would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary:

The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only shows evidence that the claimed compounds can treat cardiovascular diseases and related disorders such as various forms of hypertension, and angina. However, said evidence does not adequately guide the skilled clinician in the treatment of diseases of different etiologies such as: diabetes, retinopathy, chronic renal failure, osteoarthritis, cirrhosis, asthma, etc. due to different underlying factors. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claims 8 and 9.

Allowable Subject Matter

Claims 1-7 are allowable.

The following is a statement of reasons for the indication of allowable subject matter:

The closest reference, **Martin-Santamaria** (J. Org. Chem. 1999), discloses a compound that has been excluded by the proviso in claim 1. Furthermore, the reference does not disclose any activity for said compound, and therefore, there is no motivation for a prima facie case of obviousness.

References cited on PTO-892

The cited references are either Pregrant Publication of related applications, or show state of the art. While they teach tricyclic compounds, they fail to teach a core of pyrazolo-quinazoline-dione as claimed herein.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

5-10-05

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
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